

CLAIMS

What is claimed is:

1. A method of inducing transplant tolerance in a mammal, comprising inhibiting T-cell costimulation and IL-2 mediated T-cell proliferation without inhibiting IL-2 mediated T-cell apoptosis.
2. A method of inducing transplant tolerance in a mammal, comprising administering to said mammal an effective dose of a T-cell costimulation blockade agent and an effective dose of an immunosuppressive agent, while maintaining normal levels of T-cell death.
3. The method of Claim 2 wherein the immunosuppressive agent is rapamycin, or a biologically active derivative thereof.
4. The method of Claim 2 wherein the costimulation blockade agent and the immunosuppressive agent are administered substantially simultaneously.
5. The method of Claim 2 wherein the costimulation blockade agent and the immunosuppressive agent are administered simultaneously and subsequently the immunosuppressive agent is administered continuously at effective doses.
6. The method of Claim 2 wherein the costimulation blockade agent comprises at least one agent that blocks a signaling pathway mediated by CD40, CD40L, B7, CD28 or CTLA4.
7. The method of Claim 6 wherein the costimulation blockade agent comprises at least one agent selected from the group consisting of anti-CD40 antibodies, anti-

CD40L antibodies, anti-B7 antibodies, anti-CD28 antibodies, anti-CTLA4 antibodies, B7-Ig, CD28-Ig, CD40-Ig, CD40L-Ig, CTLA4-Ig, soluble extracellular domain proteins of CD40, CD40L, B7, CD28 and CTLA4 and derivatives thereof, and costimulation blockade drugs.

- 5 8. The method of Claim 2 wherein the costimulation blockade comprises anti-CD40L and CTLA4-Ig.
9. The method of Claim 3 wherein the rapamycin is contained in a fish oil composition.
- 10 10. The method of Claim 3 wherein the route of administration is intraperitoneal, intravenous, oral or subcutaneous.
11. A composition comprising at least one costimulation blockade agent and rapamycin, or a biologically active derivative thereof.
12. The composition of Claim 11 further comprising fish oil.
- 15 13. The method of Claim 11 wherein the costimulation blockade agent comprises at least one agent selected from the group consisting of anti-CD40 antibodies, anti-CD40L antibodies, anti-B7 antibodies, anti-CD28 antibodies, anti-CTLA4 antibodies, B7-Ig, CD28-Ig, CD40-Ig, CD40L-Ig, CTLA4-Ig; soluble extracellular domain proteins of CD40, CD40L, B7, CD28 and CTLA4 and derivatives thereof, and costimulation blockade drugs.
- 20 14. A kit comprising at least one costimulation blockade agent and rapamycin.

15. A method of inducing transplant tolerance in a mammal comprising administering a T-cell costimulation blockade agent, wherein T-cell proliferation, but not T-cell apoptosis is inhibited.
- 5 16. A method of inhibiting T-lymphocyte induced rejection of an allograft in a mammal comprising administering a T-cell costimulation blockade agent and an immunosuppressive agent, wherein T-cell costimulation and IL-2 mediated T-cell proliferation are inhibited and IL-2 mediated T-cell apoptosis is not inhibited.
- 10 17. The method of Claim 16 further comprising administering an effective dose of rapamycin or a derivative thereof.
18. A method of prolonging the survival of an allograft in a mammal, comprising administering a T-cell costimulation blockade agent and an immunosuppressive agent, wherein T-cell costimulation and IL-2 mediated T-cell proliferation are inhibited and IL-2 mediated T-cell apoptosis is not inhibited.
- 15 19. The method of Claim 18 further comprising administering an effective dose of rapamycin or a derivative thereof.
- 20 20. A method for inducing T-cell non-responsiveness to a donor tissue or organ in a recipient, comprising administering a T-cell costimulation blockade agent and an immunosuppressive agent, wherein T-cell costimulation and IL-2 mediated T-cell proliferation are inhibited and IL-2 mediated T-cell apoptosis is not inhibited.
- 20 21. The method of Claim 20 further comprising administering an effective dose of rapamycin or a derivative thereof.

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